



JUN - 5 2002

WARNING LETTER

CERTIFIED MAIL – RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

David R. Hassman, M.D.
Comprehensive Clinical Research
160 South White Horse Pike, 2nd Floor
Berlin, New Jersey 08009

Ref: 02-HFD-45-0301

Dear Dr. Hassman:

Between July 9 and 31, 2001, Mr. Shirley Isbill and Ms. Loretta Nemchik, representing the Food and Drug Administration (FDA), conducted an inspection to investigate allegations of irregularities in the conduct of investigational new drug studies for which you were the investigator of record. The FDA inspection included a review of the following clinical studies that you conducted:

Protocol [] "Comparative study of the Safety and Efficacy of Two Oral Doses of [] for the Treatment of Community-Acquired Pneumonia," sponsored by []

Protocol [] "Comparative study of the Safety and Efficacy of [] 150 mg QD vs. 150 mg of BID for the Treatment of Acute Bacterial Sinusitis," sponsored by []

Protocol [] "A Randomized, Controlled Study of Tamiflu Used for the Prevention of [] in Families," sponsored by Roche Global Development.

Protocol [] "A Double-Blind Placebo-Controlled Dose-Finding Trial to Evaluate the Efficacy and Safety of [] in Subjects with Symptoms of Gastroesophageal Reflux Disease (GERD)," sponsored by []

This inspection is part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects in those studies are protected.

From our evaluation of the inspection report, the documents submitted with that report, and your written response dated August 13, 2001, we conclude that you did not adhere to pertinent federal regulations governing the conduct of clinical investigations. At the conclusion of the inspection our personnel presented to you, and Ms. [] your Director of Regulatory Affairs and Quality Assurance, the items listed on the Form FDA 483, Inspectional Observations. We note your responses and accept your explanations to all items except items 1 and 5 on the Form FDA 483. We wish to emphasize the following:

1. FAILURE TO ADEQUATELY SUPERVISE THE CLINICAL INVESTIGATION [21 CFR 312.60]

The investigator agreement you signed requires you to personally conduct or supervise the clinical investigation (see FDA Form 1572). FDA's investigation revealed that you failed to adequately supervise those aspects of clinical investigations which you did not personally conduct. As described in more detail below, this lack of supervision resulted in submission of false information to the sponsor and failure to maintain adequate and accurate case histories. Although authority may be delegated, it is the principal investigator who is ultimately responsible for the conduct of the study.

2. SUBMISSION OF FALSE INFORMATION TO THE SPONSOR [21 CFR 312.70]

In Protocol [] you submitted false information to the sponsor for subject #30691. Page 20 of the case report form (CRF) indicates that the nasal swab culture for Visit 4 was done on 3/5/01. However, FDA's investigation revealed that the study subject did not visit your study site or provide a nasal swab sample on 3/5/01. We learned during the inspection that Ms. [] (your lead clinical study coordinator) requested Ms. [] (the study coordinator for protocol []) to fabricate the subject's nasal swab. Ms. [] has acknowledged that a nasal swab from her own nose was misrepresented as the swab obtained from the study subject on 3/5/01.

3. FAILURE TO MAINTAIN ADEQUATE AND ACCURATE CASE HISTORIES [21 CFR 312.62(b)]

In your written response you acknowledged that in protocol [] for subjects #6420 and #6421, Ms. [] (the study coordinator) prepared laboratory requisitions, source worksheets that included vital signs, and completed CRFs, prior to the subjects' visits. For example, the data pertaining to the collection of blood sample on 2/22/01, which was reported on page 108 of each subject's CRF, were misrepresented. FDA's investigation revealed that both subjects did not provide a blood sample on 2/22/01 as initially reported on their respective case report forms. We note that the information regarding the blood sample collections was corrected at a later date, and that the misrepresented vital signs data were not submitted to the sponsor. Nevertheless, the practice of recording data for study subjects prior to their actual study visits is unacceptable.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational drugs. As the investigator of record, it is your responsibility to ensure adherence to FDA regulations. Specifically, your responsibilities include the maintenance of all study-related documents.

Because of the serious nature of the violations of FDA regulations discussed above, we request that you notify this office, in writing, within 15 working days of your receipt of this letter, the specific steps that you have taken or plan to take to prevent similar violations in the future. Failure to promptly respond to this letter may result in further regulatory action. Your written response and any pertinent documentation should be addressed to the address shown below:

Antoine El Hage, Ph.D.
Associate Director
Good Clinical Practice Branch I & II, HFD-46 & 47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Suite 125
Rockville, MD 20855

Sincerely yours,

A handwritten signature in cursive script that reads "Joanne L Rhoads M.D.".

Joanne L. Rhoads, M.D., M.P.H.
Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research